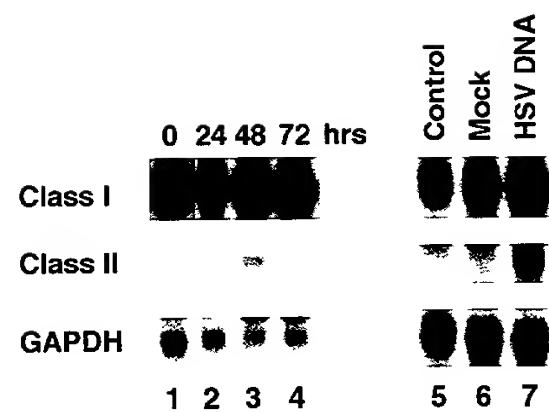
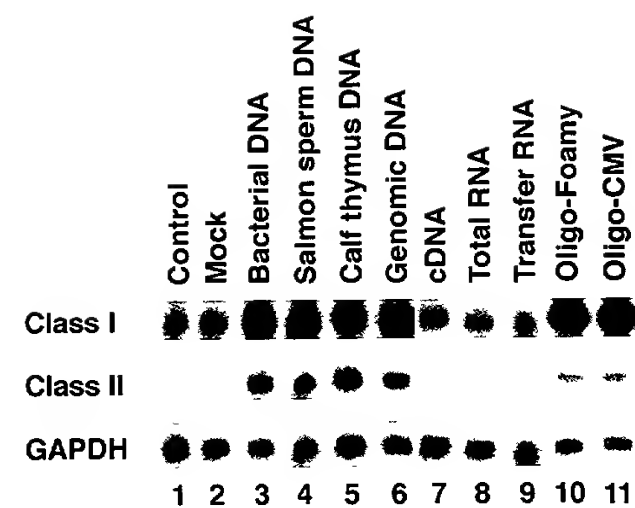


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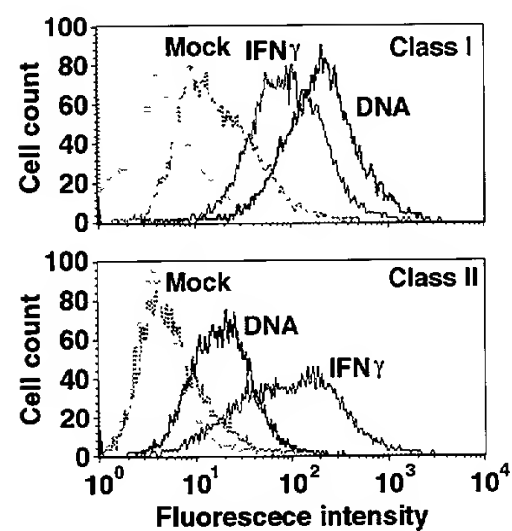
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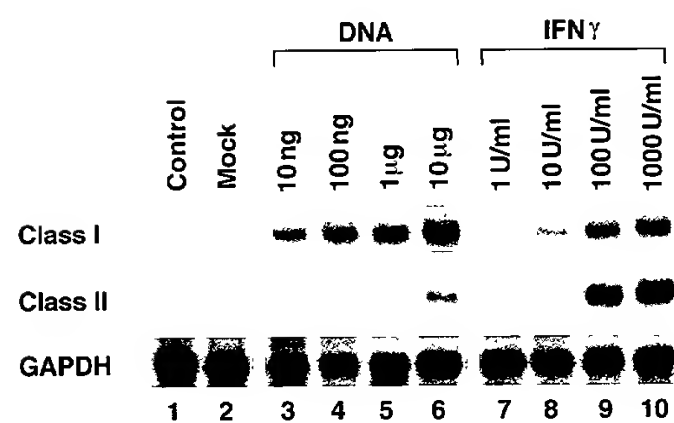
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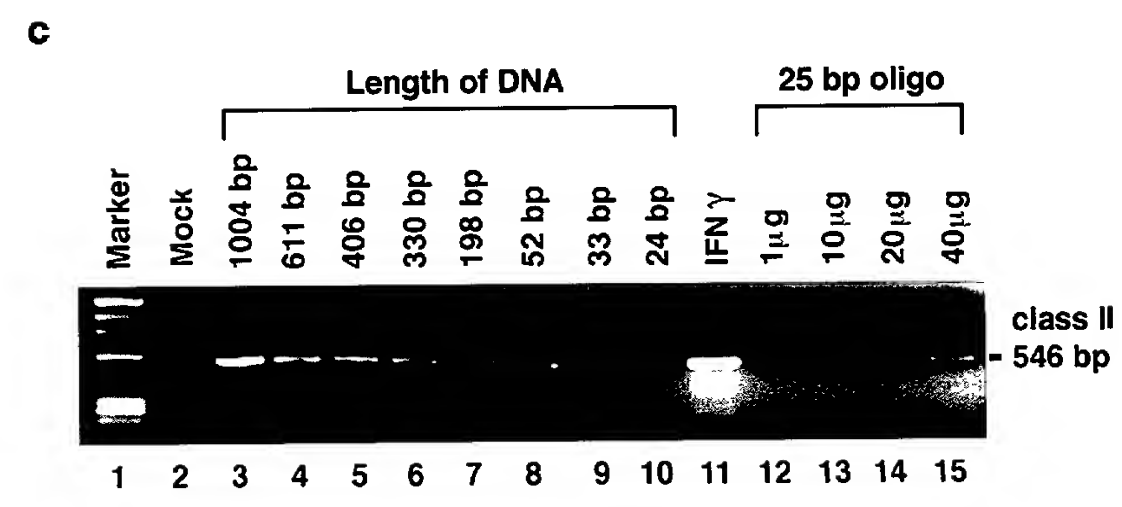
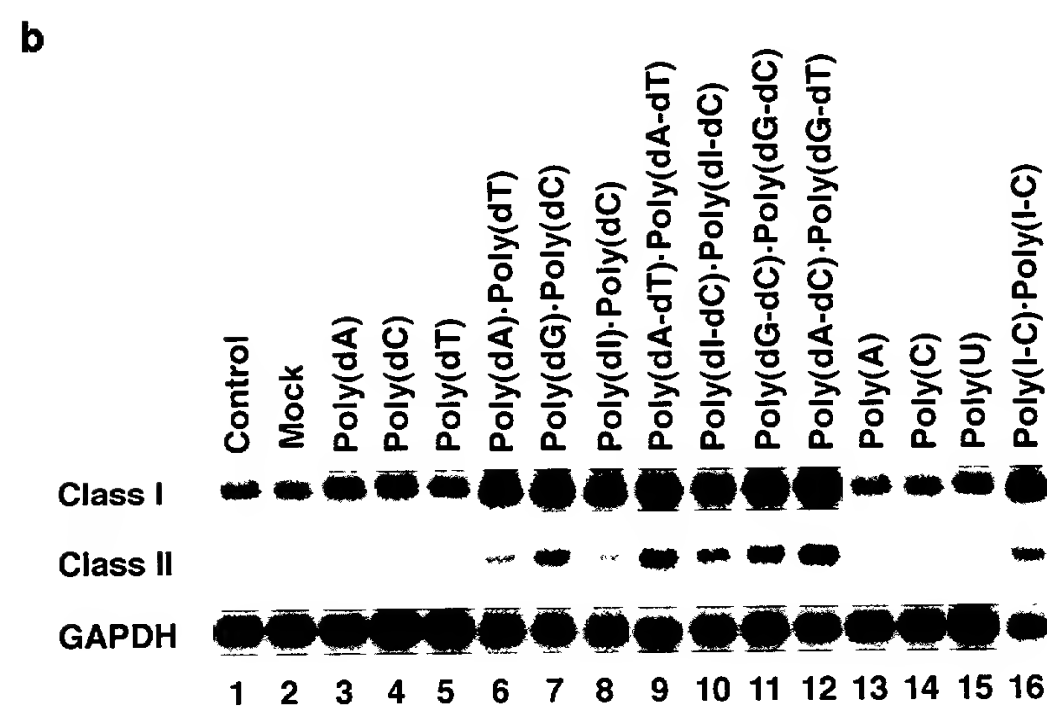
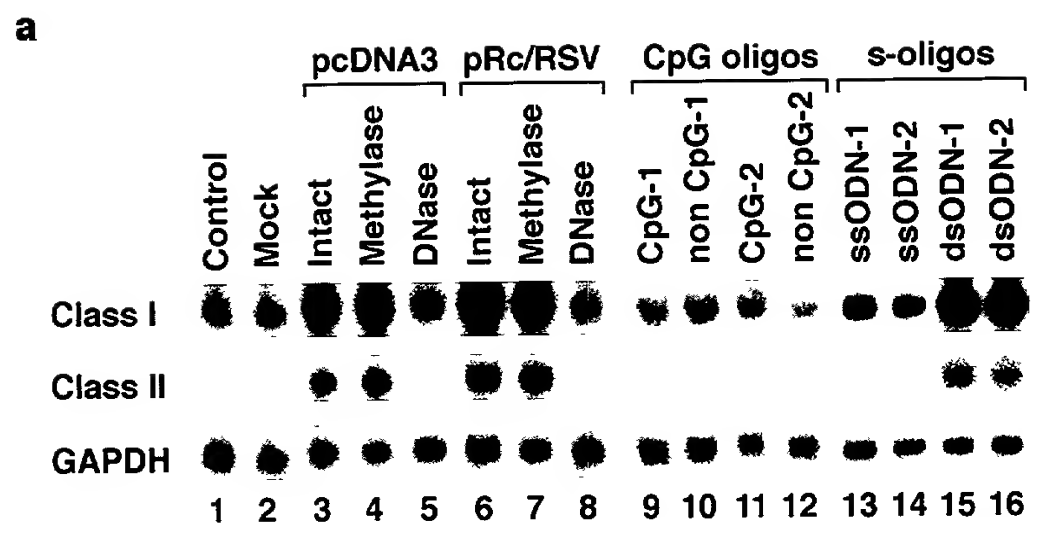
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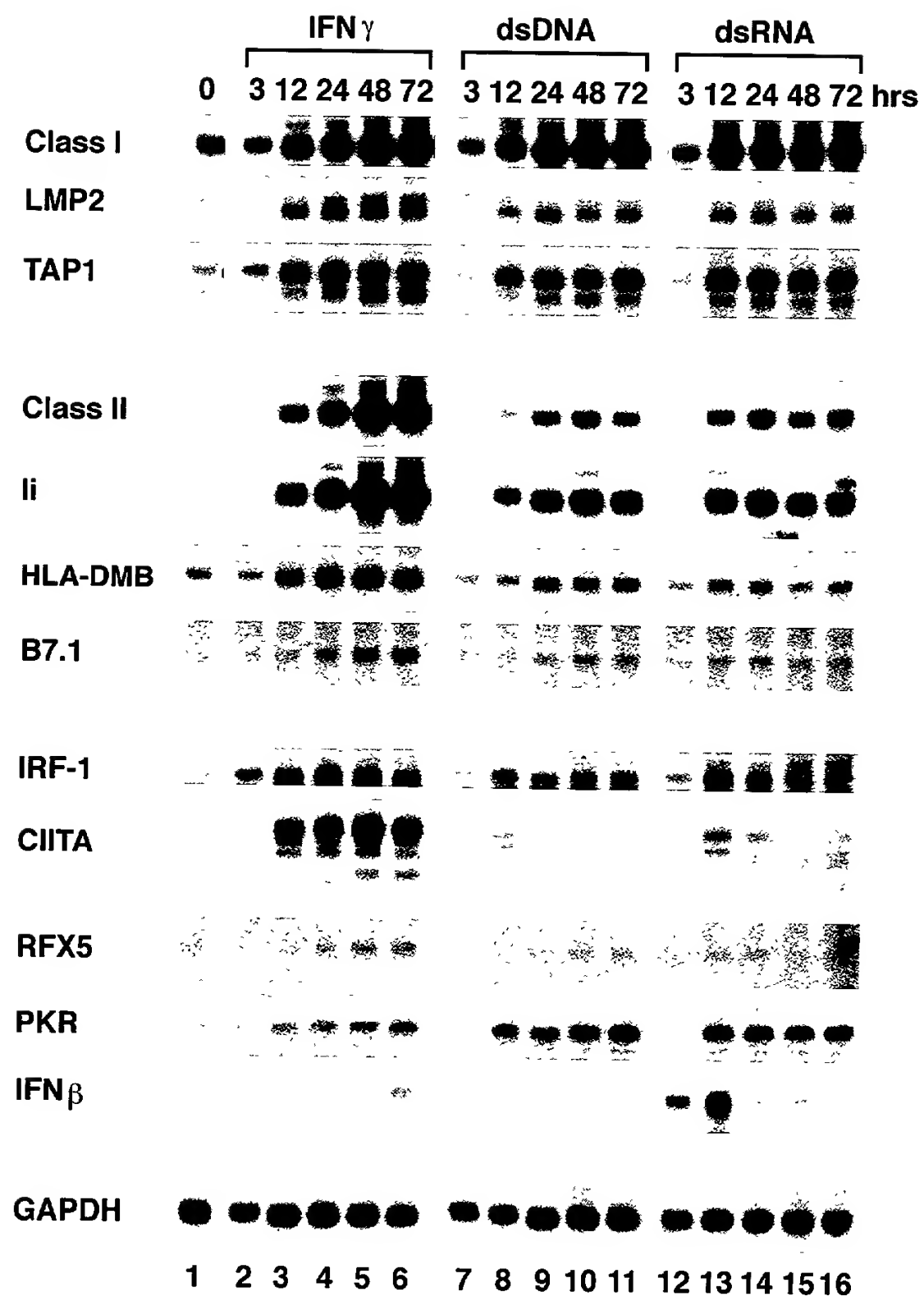


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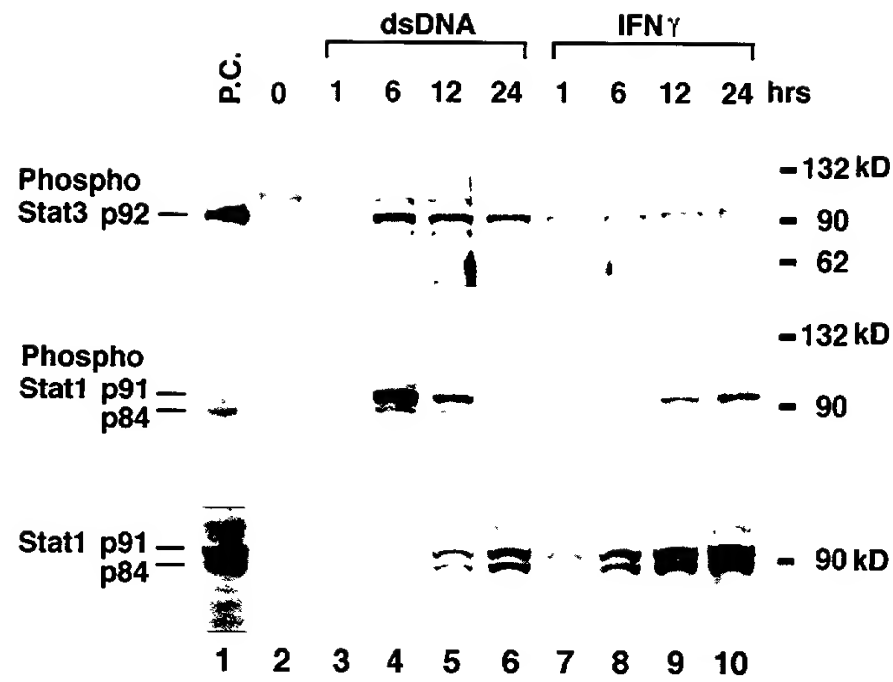


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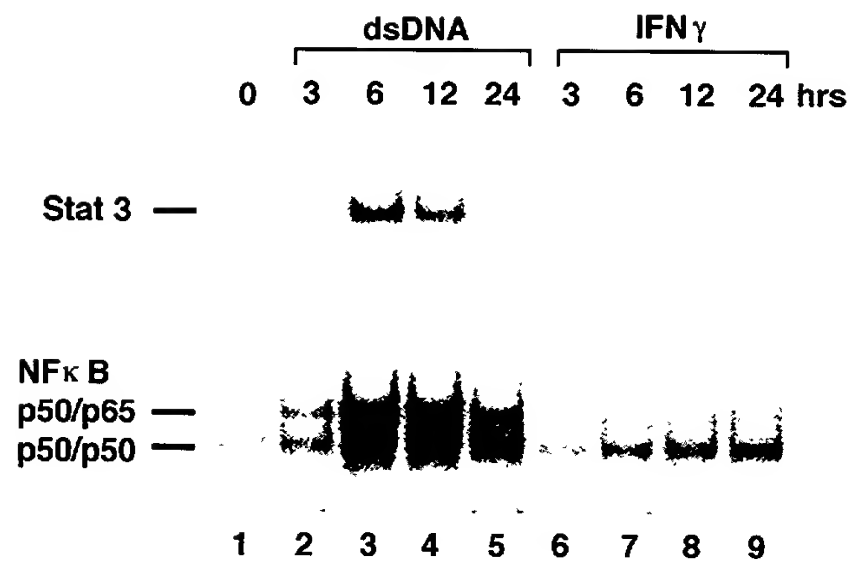




a



b

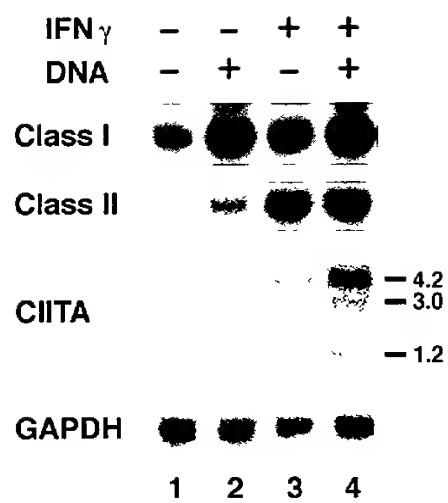


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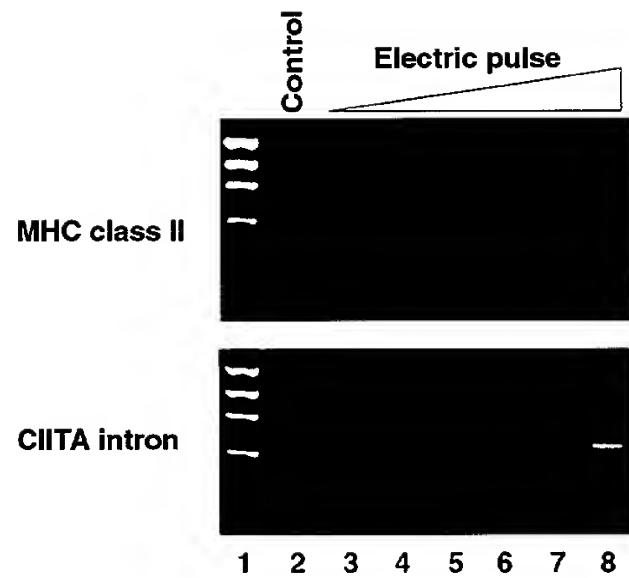


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a

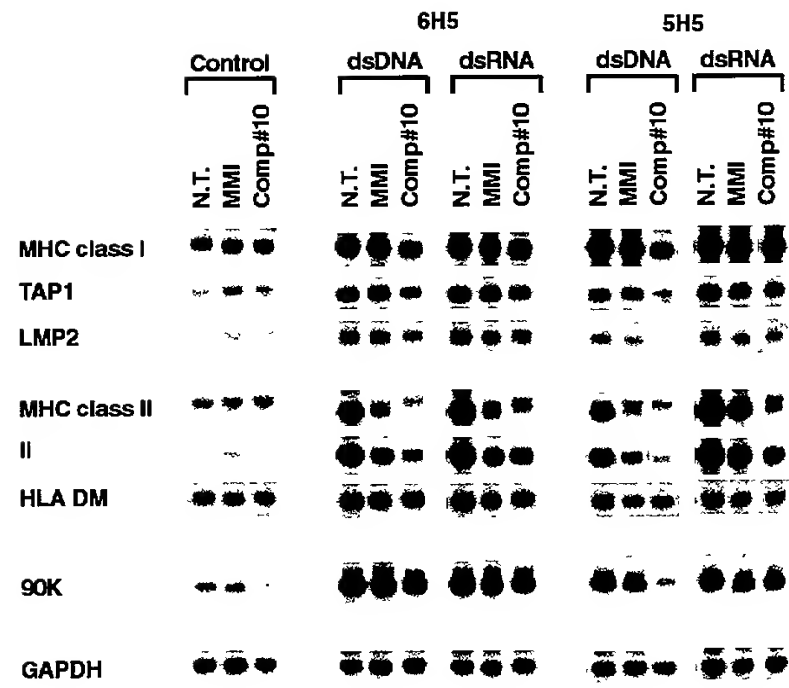


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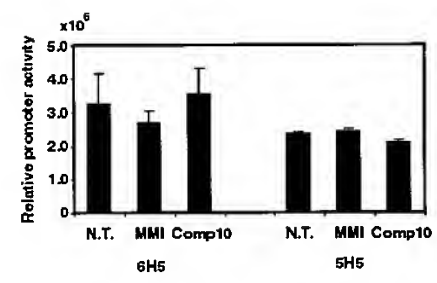


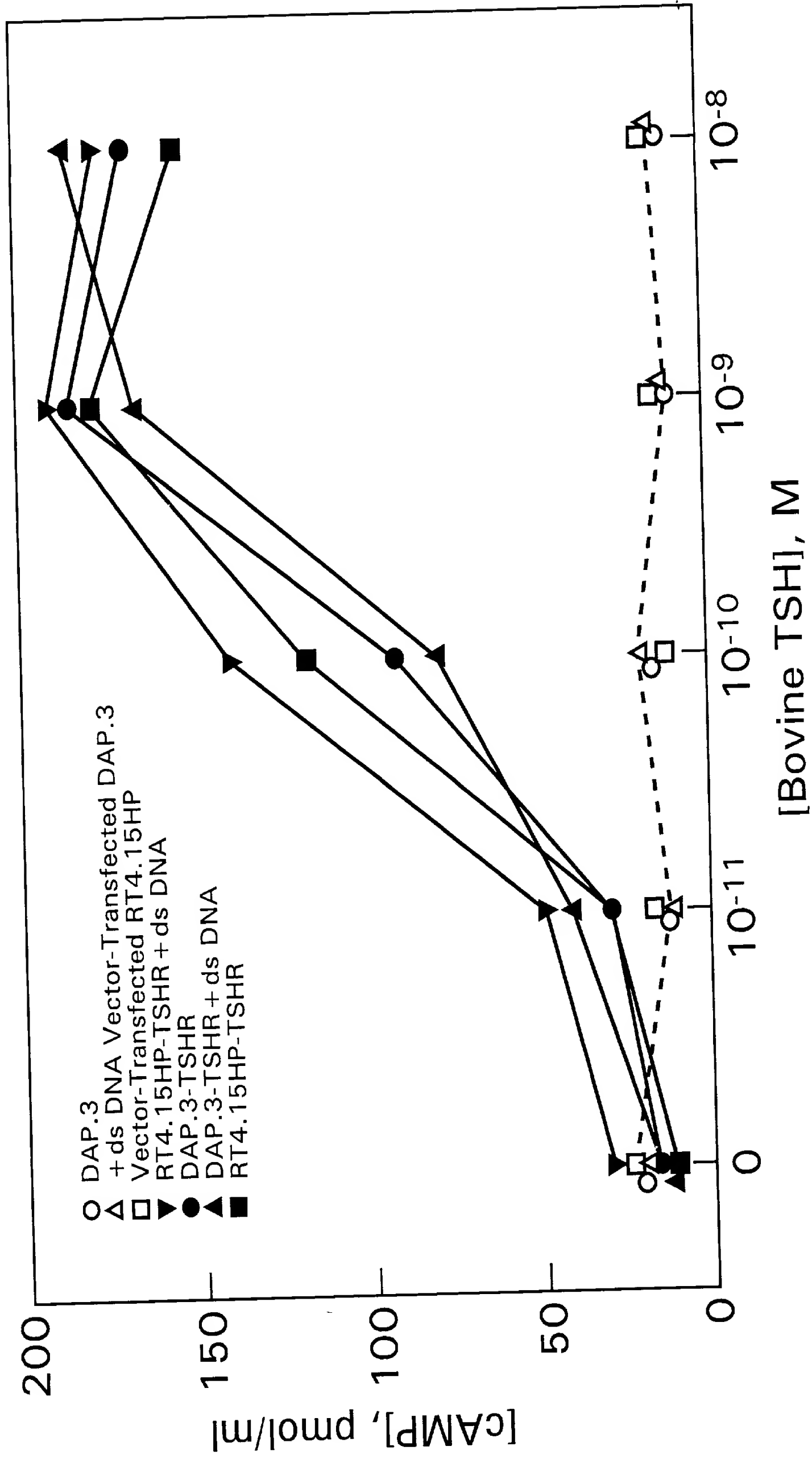
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a



b



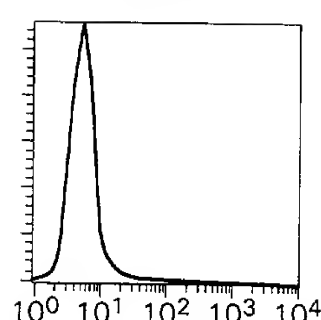
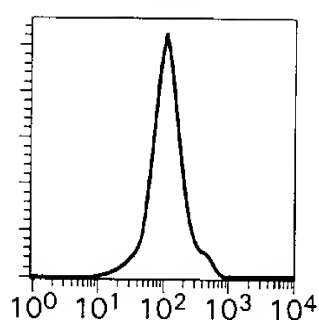
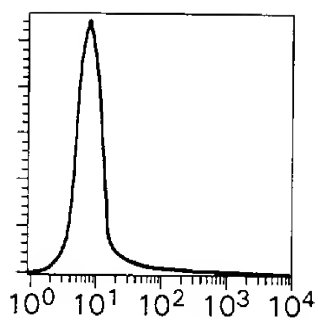


Control

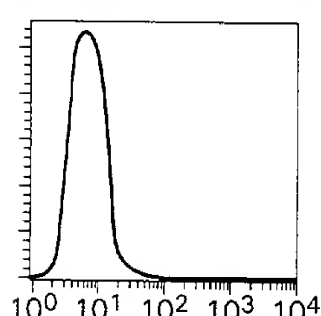
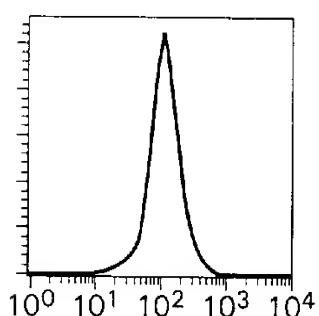
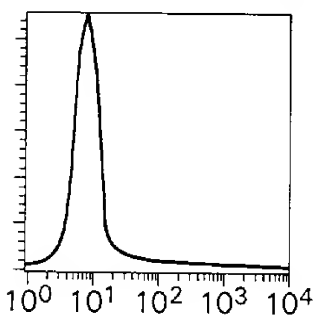
Class I

Class II

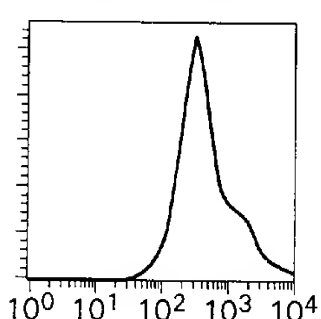
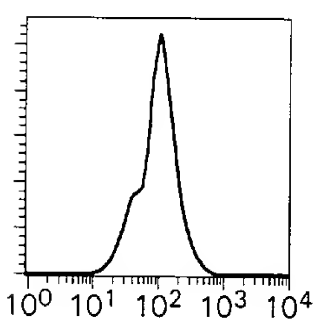
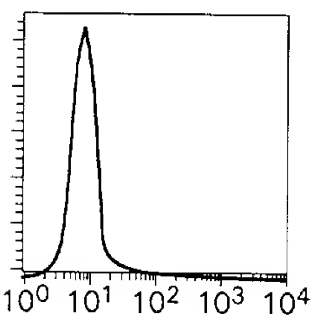
Control
DAP.3



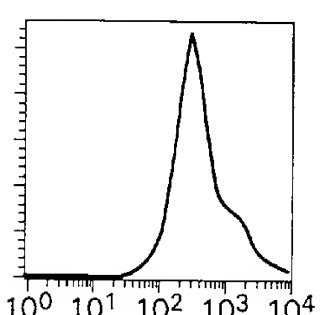
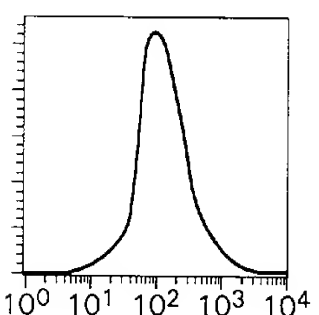
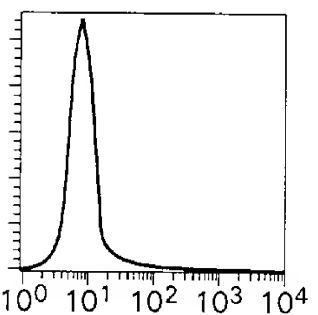
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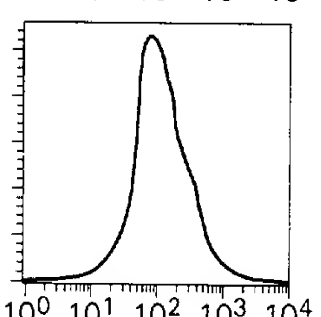
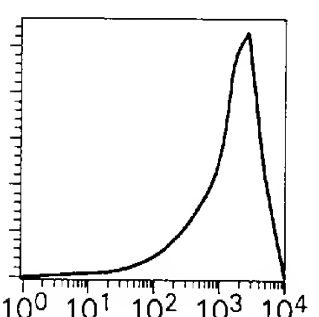
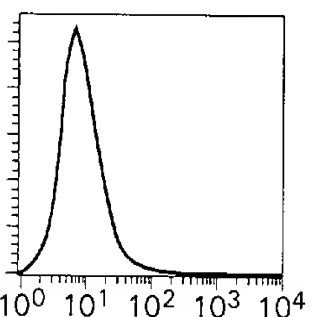
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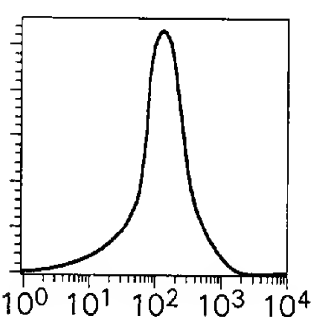
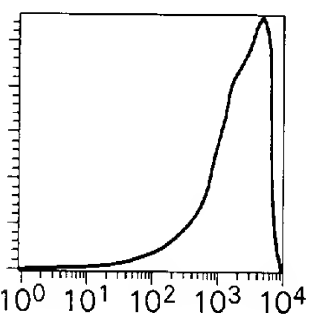
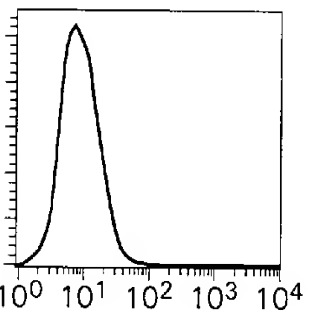
hTSHR
Transfected
RT4.15HP



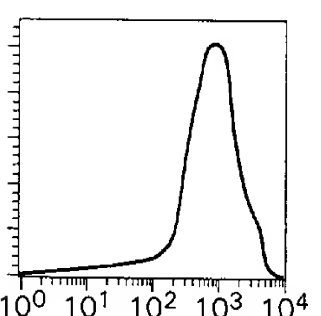
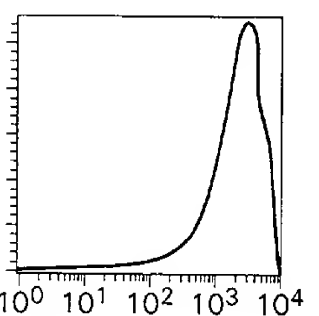
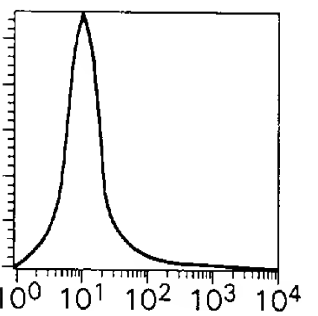
dsDNA
Transfected
DAP.3



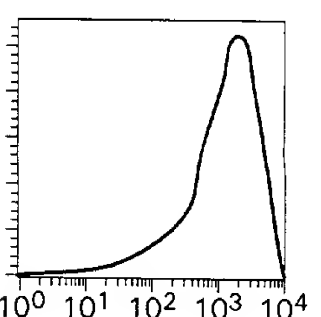
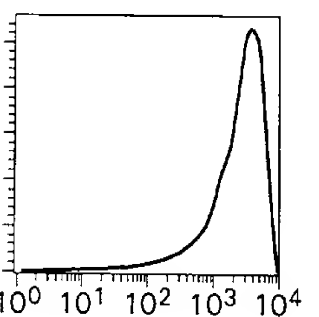
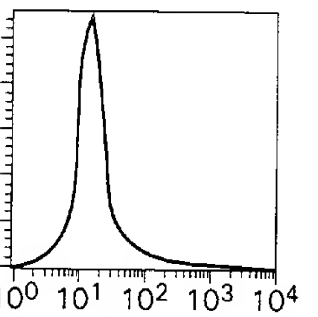
dsDNA
Transfected
hTSHR DAP.3



dsDNA
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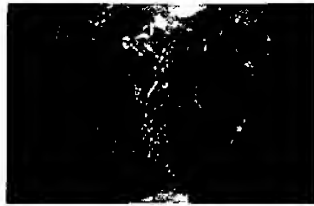
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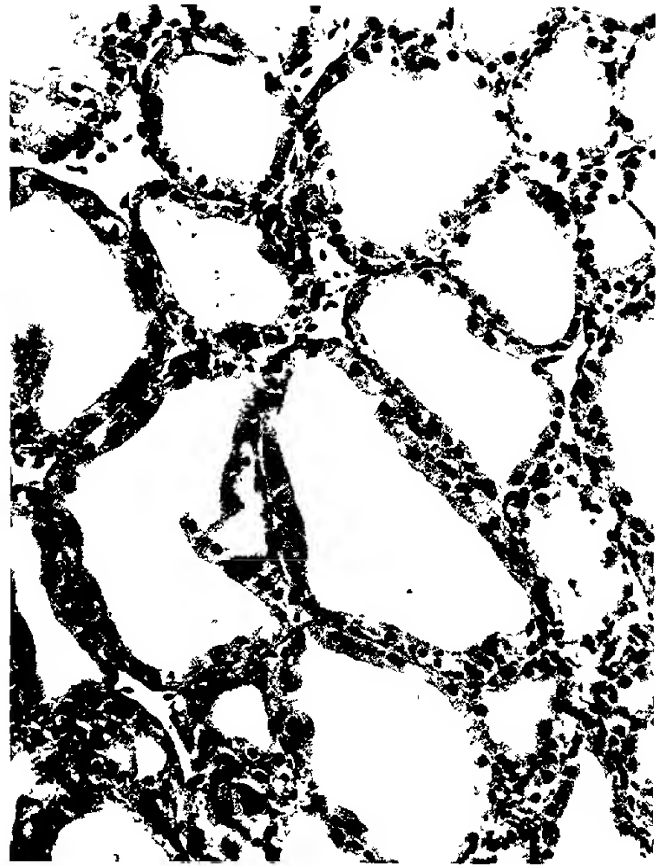
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0.00000000005581299774348736 0.00000000002790649887174368 0.00000000001395324943587184 0.00000000000697662471793592 0.00000000000348831235896796 0.00000000000174415617948398 0.00000000000087207808974199 0.000000000000436039044870995 0.0000000000002180195224354975 0.00000000000010900976121774875 0.00000000000005450488060887438 0.00000000000002725244030443719 0.000000000000013626220152218595 0.0000000000000068131100761092975 0.0000000000000034065550380546488 0.0000000000000017032775190273244 0.0000000000000008516387595136622 0.0000000000000004258193797568311 0.00000000000000021290968987841555 0.00000000000000010645484493920778 0.00000000000000005322742246960389 0.000000000000000026613711234801945 0.000000000000000013306855617400972 0.000000000000000006653427808700486 0.000000000000000003326713904350243 0.0000000000000000016633569521751215 0.0000000000000000008316784760875608 0.0000000000000000004158392380437804 0.0000000000000000002079196190218902 0.0000000000000000001039598095109451 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Mice Immunized with
ds DNA-Transfected
hTSHR DAP.3 Cells

A.



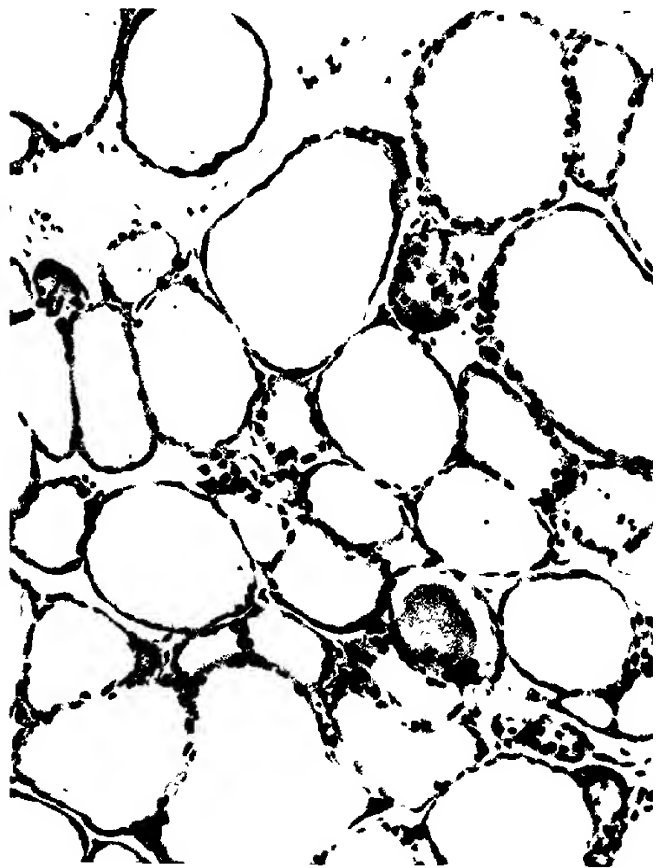
B.



C.

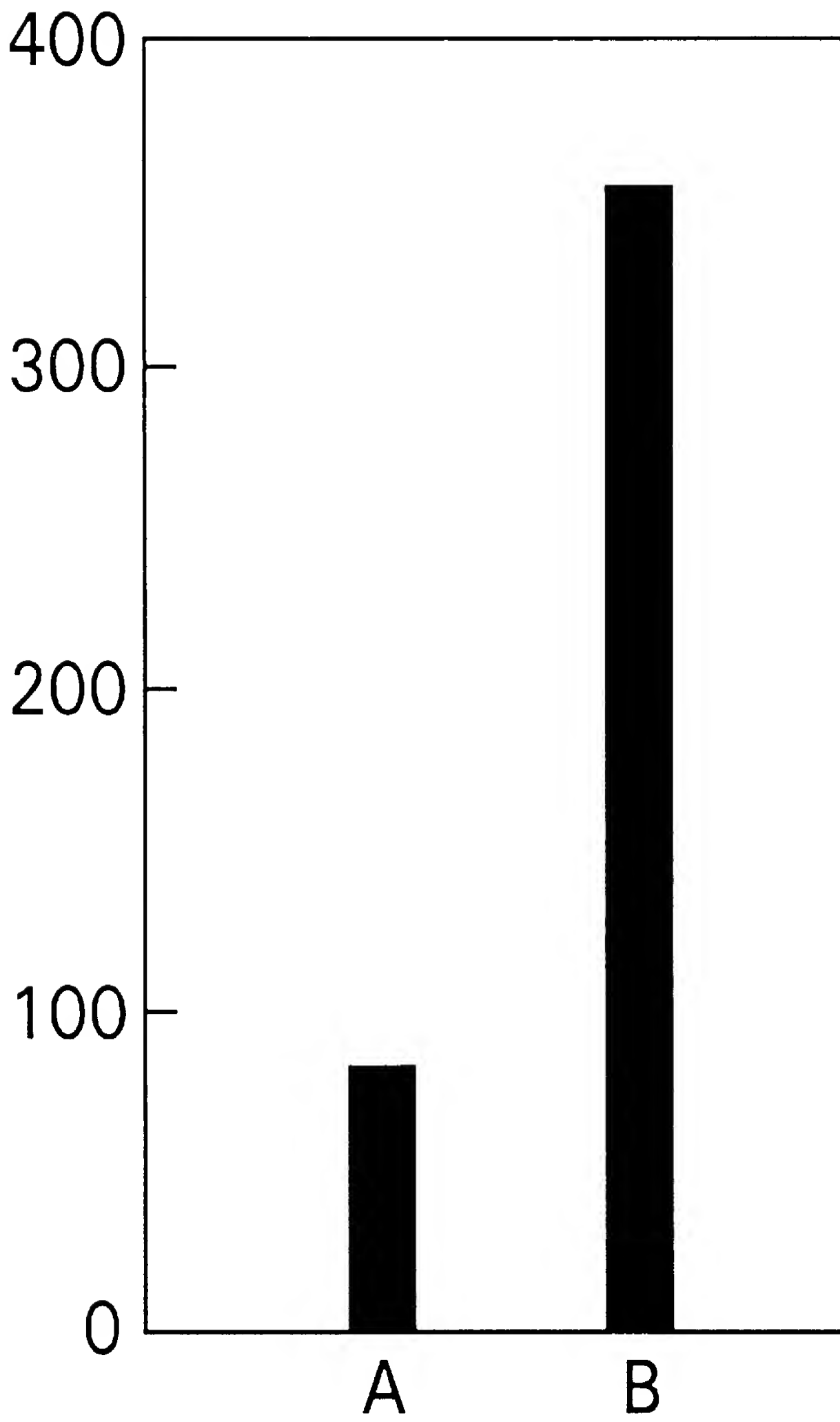


D.



1000 800 600 400 200 0

%INCREASE
IN cAMP PRODUCTION



10 20 30 40 50 60 70 80 90 100
 gaattctacg ccaggcaATG GCTCTTCTGT GGCTCCTCTC TGTGTTCTTG CTGGTTCCAG GGAAGTCAAGG TGCAAAGGAT GGAGACATGC GCCTGGTTAA 100
 [MetA] laLeuLeuTr pLeuLeuSer ValPheLeuL euValProGl yThrGlnGly AlaLysAspG l yAspMetAr gLeuValAs
 TGGGGCCTCA CCCAGTGAGG GCCGCGTGA GATCTTCTAC AGAGGCCGGT GGGGGACACT GTGCGACAAC CTCTGGAACC TTTTGGATGC CCACGTCTTC 200
 nGlyAlaSer ProSerGluG lyArgValGI ullePheTyr ArgGlyArgT rpGlyThrLe uCysAspAsn LeuTrpAsnL euLeuAspAl aHisValPhe
 TGCCGGGCCC TGGGCTATGA TAATGCTACT CCAGCACTGA ACAGAGTCGC CTTCGGGGCCA GGAAAGGGAC CAATCATGCT GGATGAGGTG GAATGCACAG 300
 CysArgAlaL euGlyTyrAs pAsnAlaThr ProAlaLeuA snArgValAl aPheGlyPro GlyLysGlyP rolleMetLe uAspGluVal GluCysThrG
 GGAACGAGTC GTCACTGGCC AATTGCAGCT CCCTGGGCTG GATGGTGAGC CACTGCGGGC ATGAGAAGGA CGCGGGCGTG GTCTGCTCCA ACGATTCCAG 400
 ly(Asn)GluSe rSerLeuAla (Asn)CysSerS erLeuGlyTr pMetValSer HisCysGlyH isGluLysAs pAlaGlyVal ValCysSer(A sn)AspSerAr
 GGGCATTAC ATCCTAGACC TCTCTGGAGA GCTTCCAGAT TCACTGGGCC AGATCTTTGA CAGCCAGCAG GACTGCGACC TGTTCATCCA GGTGACAGGG 500
 gGlylleHis lleLeuAspL euSerGlyGI uLeuProAsp SerLeuGlyG inllePheAs pSerGlnGln AspCysAspL euPheilleGI nValThrGly
 CAGGGACATG GGGACCTGAG CCTCTGTGCC CACACACTGA TCCTGCGCAC CAACCCCGAG GCCCAGGCC TGTGGCAAGT GGTGGGCAGC AGTGTCTATCA 600
 GlnGlyHisG lyAspLeuSe rLeuCysAla HisThrLeul leLeuArgTh rAsnProGlu AlaGlnAlaL euTrpGlnVa lValGlySer SerValilleM
 TGAGAGTGGA CGCTGAGTGC ATGCCTGTGC TCAGAGACTT CCTCAGGTAC TTTTACTCCC GAAGAATCGA GGTCAGCATG TCTTCTGTCA AGTGTCTGCA 700
 etArgValAs pAlaGluCys MetProValV alArgAspPh eLeuArgTyr PheTyrSerA rgArgilleGI uValSerMet SerSerValL ysCysLeuHi
 CAAGCTGGCC TCCGCTATG GAGCCACAGA GCTCCAGGGT TACTGTGGAC GGCTTTTTGT CACCCTCCTC CCCCAGGACC CCACCTTTCCA TACGCCCTG 800
 sLysLeuAla SerAlaTyrG lyAlaThrGI uLeuGlnGly TyrCysGlyA rgLeuPheVa lThrLeuLeu ProGlnAspP roThrPheHi sThrProLeu
 GAACCTTACG AGTATGCGCA GGCCACCGGG GACTCTGTGC TGGAAGATCT GTGTGTGCAA TTCCTGGCCT GGAACCTCGA GCCTCTGACA CAGGCCGAGT 900
 GluLeuTyrG luTyrAlaGI nAlaThrGly AspSerValL euGluAspLe uCysValGln PheLeuAlaT rpAsnPheGI uProLeuThr GlnAlaGluS
 CCTGGTTGTC TGTTCCTCAAT GCCTTGATCC AAGCTCTCCT CCCCAGAGC GAGCTGGCTG TGTCTAGTGA ACTGGATTG CTGAAGGCAG TGGACCAGTG 1000
 erTrpLeuSe rValProAsn AlaLeulleG inAlaLeuLe uProLysSer GluLeuAlaV alSerSerGI uLeuAspLeu LeuLysAlaV alAspGlnTr
 GAGCACAGCG ACCGGCGCCT CCCACGGGGA TGTAAGCGC CTGGTGAAC AGATCCGCTT TCCTATGATG CTGCCCCAGG AGCTGTTTGA GCTACAGTTC 1100
 pSerThrAla ThrGlyAlaS erHisGlyAs pValGluArg LeuValGluG inlleArgPh eProMetMet LeuProGlnG luLeuPheGlu LeuGlnPhe
 AACCTGTCTT TGTACCAAGG TCACCAGGCC CTGTTCCAGA GGAAGACCAT GGAGGCCCTG GAGTTCCACA CAGTGCCTCT CAAAGTGCTG GCCAAGTACA 1200
 (Asn)LeuSerL euTyrGlnGI yHisGlnAla LeuPheGlnA rgLysThrMe tGluAlaLeu GluPheHisT hrValProLe uLysValLeu AlaLysTyrA
 GAAGCCTGAA CCTACCGAG GATGTCTACA AACCCCGGCT TTACACCTCT TCTACCTGGA GTAGCCTGCT GATGGCCGGT GCCTGGAGTA CACAAAGCTA 1300
 rgSerLeu(Asn)LeuThrGlu AspValTyrL ysProArgLe uTyrThrSer SerThrTrpS erSerLeuLe uMetalaGly AlaTrpSerT hrGlnSerTy
 CAAATACAGA CAGTTCTACA CATACAACTA TGGCTCACA TCCCCTACA GCAGCTACCA GAACTTCCAG ACCCCACAAC ACCCCAGCTT CCTCTTCAAG 1400
 rLysTyrArg GlnPheTyrT hrTyrAsnTy rGlySerGln SerArgTyrS erSerTyrGI nAsnPheGln ThrProGlnH isProSerPh eLeuPheLys
 GACAAGCTGA TCTCCTGGTC AGCCACCTAC CTCCCCACCA TCCAGAGTTG CTGGAAGTAT GGCTTCTCGT GTACCTCTGA CGAGCTCCCT GTACTGGGCC 1500
 AspLysLeul leSerTrpSe rAlaThrTyr LeuProThrI leGlnSerCy sTrpAsnTyr GlyPheSerC ysThrSerAs pGluLeuPro ValLeuGlyL
 TCACCACATC CAGTTACTCC GATCCAATA TCGGCTACGA GAACAAAGCG CTGATCCTCT GTGGAGGCTA CAGTGTGGTA GATGTCACCA CTTTATAGG 1600
 ueThrThrSe rSerTyrSer AspProThrI leGlyTyrGI uAsnLysAla LeulleLeuC ysGlyGlyTy rSerValVal AspValThrT hrPheilleGI
 CTCTAAGGCC CCTATTCCAG GTACCCAGGA GACCAATAGT TCCAAGACCC CCTCCCTCTT TCCCTGTGCC TCAGGGGCCT TCAGCAGCTT CCGCGTGGTC 1700
 ySerLysAla ProlleProG lyThrGlnGI uThr(Asn)Ser SerLysThrP roSerLeuPh eProCysAla SerGlyAlaP heSerSerPh eArgValVal
 ATCCGCCCCT TCTACCTCAC CAACTCCACT GACACGGAGT AGatggtaca tctcagcggg ggggactcag acattcctgt gttccctcct tggcctccag 1800
 lleArgProP heTyrLeuTh r(Asn)SerThr AspThrGlu
 cctctctgta ggaacctcca gcagcctgcc accagatttc ccttagcttc cactgtctcc atgagcttta aatgtatcta gaaggtttca gccagtactc 1900
 actcctagat ctgagagtct caggccccca attgtaggca gcaaggaggt cctgtgggat tccccatcag tcacagtcac taatctgaaa tcattaaagt 2000
 ggcaagtgct tctcgg

h90K
r90K
mama

TPRL
MALWL
MALWL

FWLL
VFWLL
VFWLL

AGLL
PAGLL
PAGLL

GTGG
GTGG
GTGG

VNDG
VNDG
VNDG

ADGDMRL
VNDGDMRL
VNDGDMRL

GGAT
GGAT
GGAT

NSPSE
NSPSE
NSPSE

QGRVE
QGRVE
QGRVE

IFRYR
IFRYR
IFRYR

QWGT
QWGT
QWGT

VYCD
VYCD
VYCD

50
50
50

h90K	NLWD	LD	TD	AS	VC	CR	AL	GF	FE	QA	AL	GR	AA	FG	QG	SG	PI	ML	DE	VE	CT	GT	ES	AS	SL	100	
r90K	NLWN	LL	DA	SH	VF	CR	AL	GY	ED	NA	TP	AL	RV	AF	GP	GG	PI	ML	DE	VE	CT	GT	ES	AS	SL	100	
mama	NLWN	LL	DA	SH	VF	CR	AL	GY	ED	NA	TP	AL	GR	AA	FG	QG	SG	PI	ML	DE	VE	CT	GT	ES	AS	SL	100

h90K	r90K	mama
A	D	A
C	C	A
K	S	S
S	S	C
S	S	R
L	S	S
G	L	L
W	G	G
L	M	M
K	V	V
S	S	S
S	R	S
N	C	R
C	H	C
R	E	G
H	H	H
E	K	E
K	K	K
D	D	D
A	A	D
G	G	A
V	V	G
V	V	V
C	C	V
S	S	C
T	N	S
N	D	N
E	T	D
T	R	T
S	S	T
T	R	T
H	G	G
H	L	L
I	I	I
L	L	L
D	D	D
L	L	L
S	S	S
G	G	G
E	E	E
L	L	L
S	S	S
E	E	E
L	L	L
S	S	S
D	D	D
A	A	A
L	L	L
G	G	G
I	I	I
F	F	F
D	D	D
S	S	S
S	S	S
Q	Q	Q

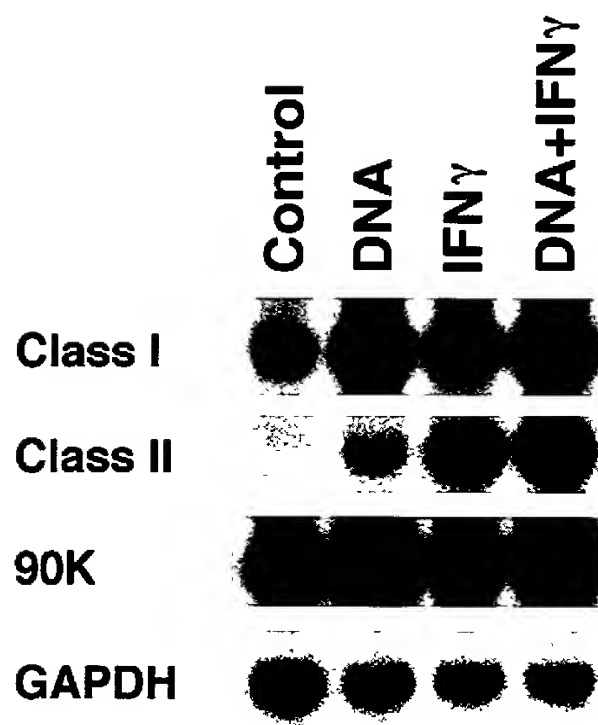
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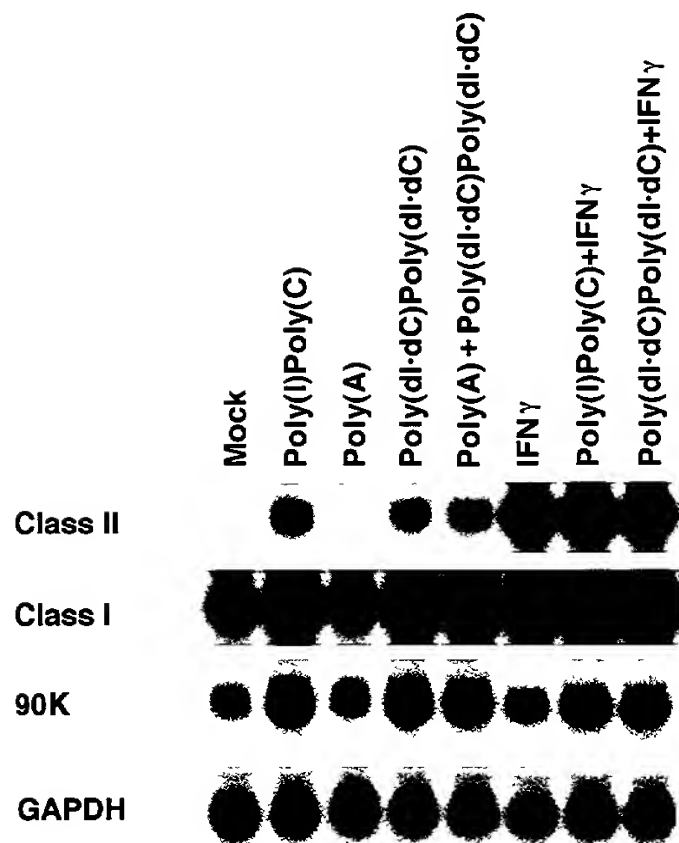
h30K 300
r90K 300
mama 300

REFPM
KIRFPM
QV
LVEE
GRLVE
EVER
EYED
SHED
ASH
GERAT
SWGST
TWST
DQWSD
VD
KAVD
LLKAVD
ALLKAVD
SEL
PSSSEL
LAVS
SE
DE
SS
PK
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QA
LQAL
IDLT
NALT

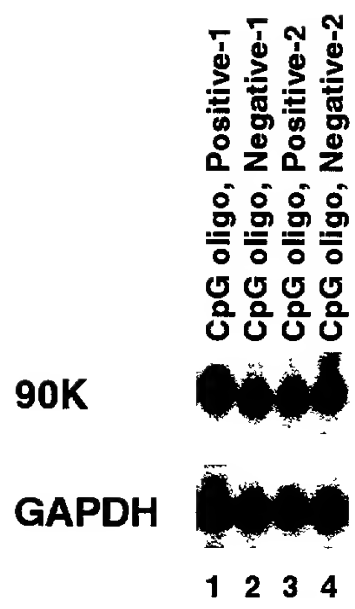
350
350
350

[illegible][illegible][illegible][illegible][illegible]

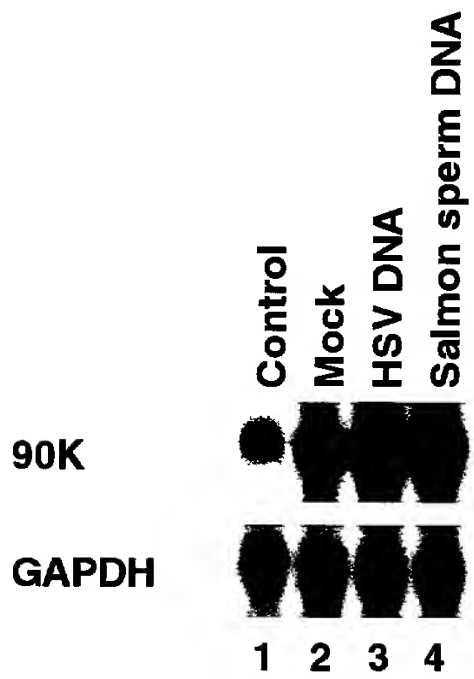


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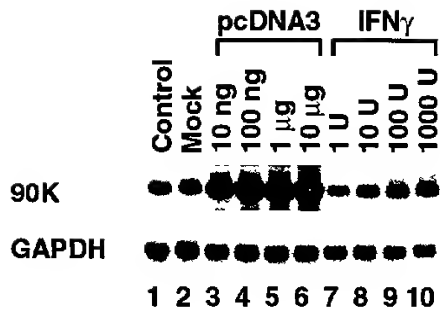
A



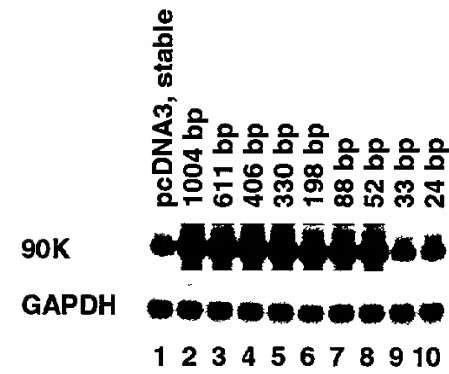
B



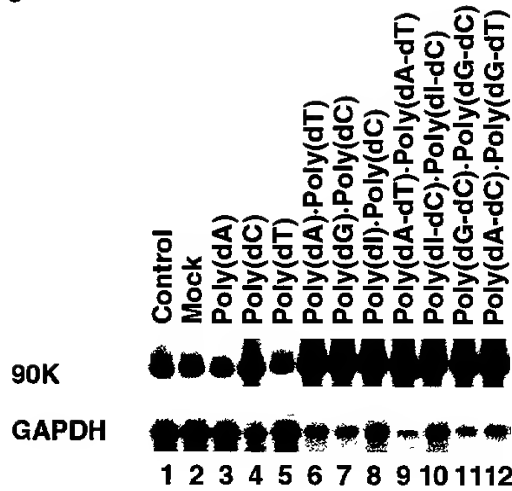
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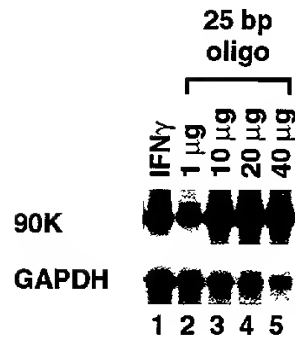
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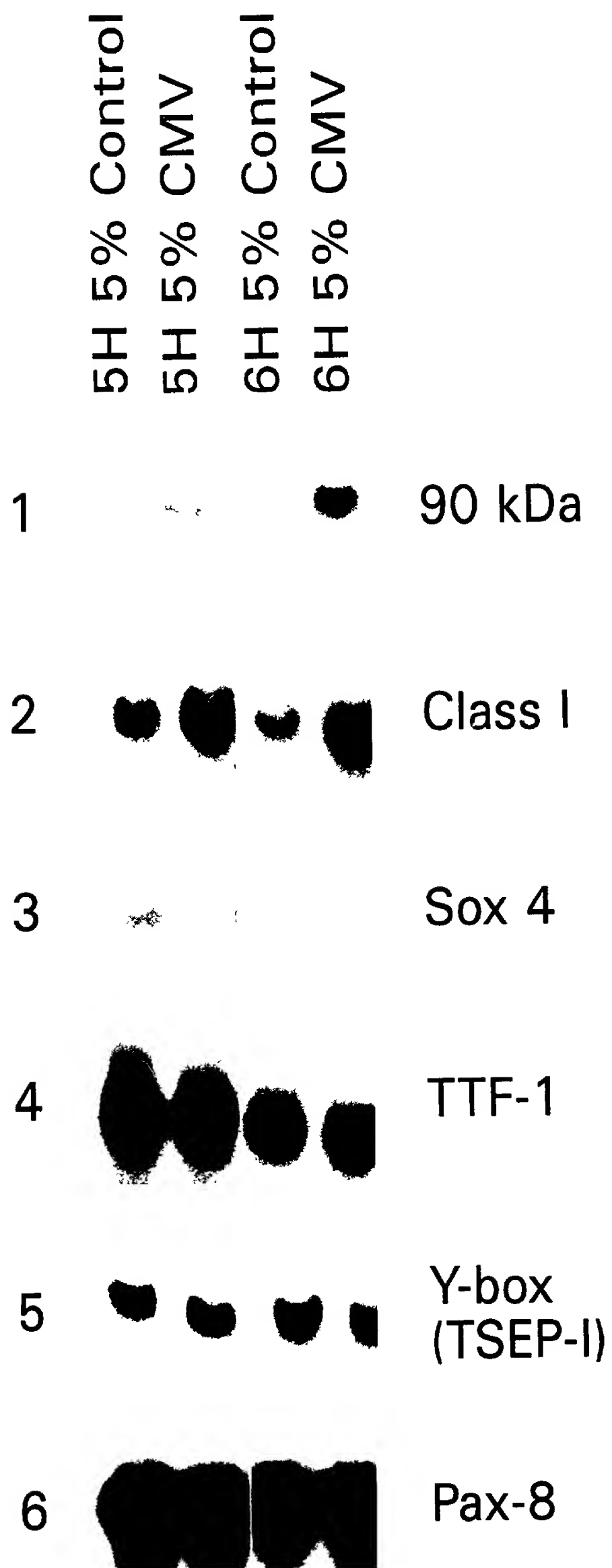


C

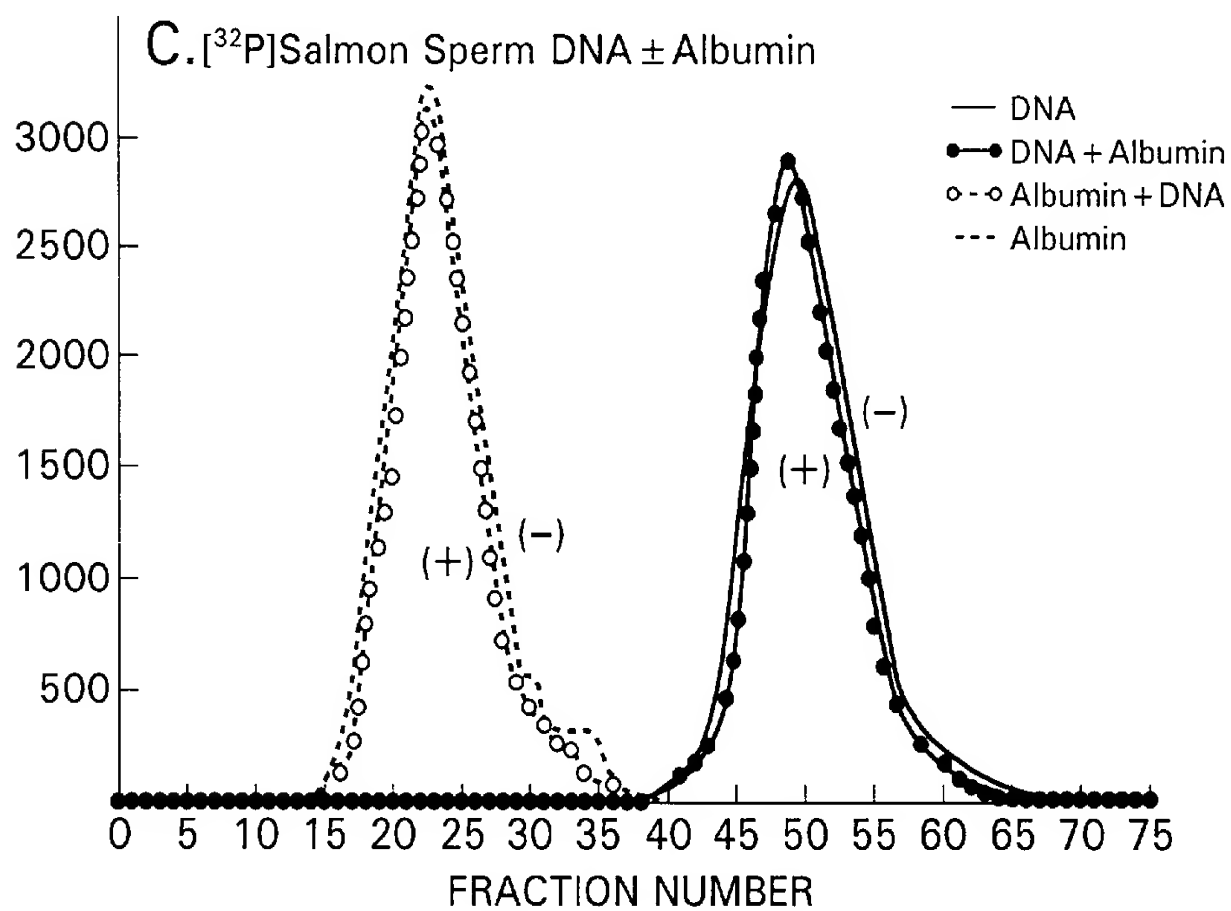
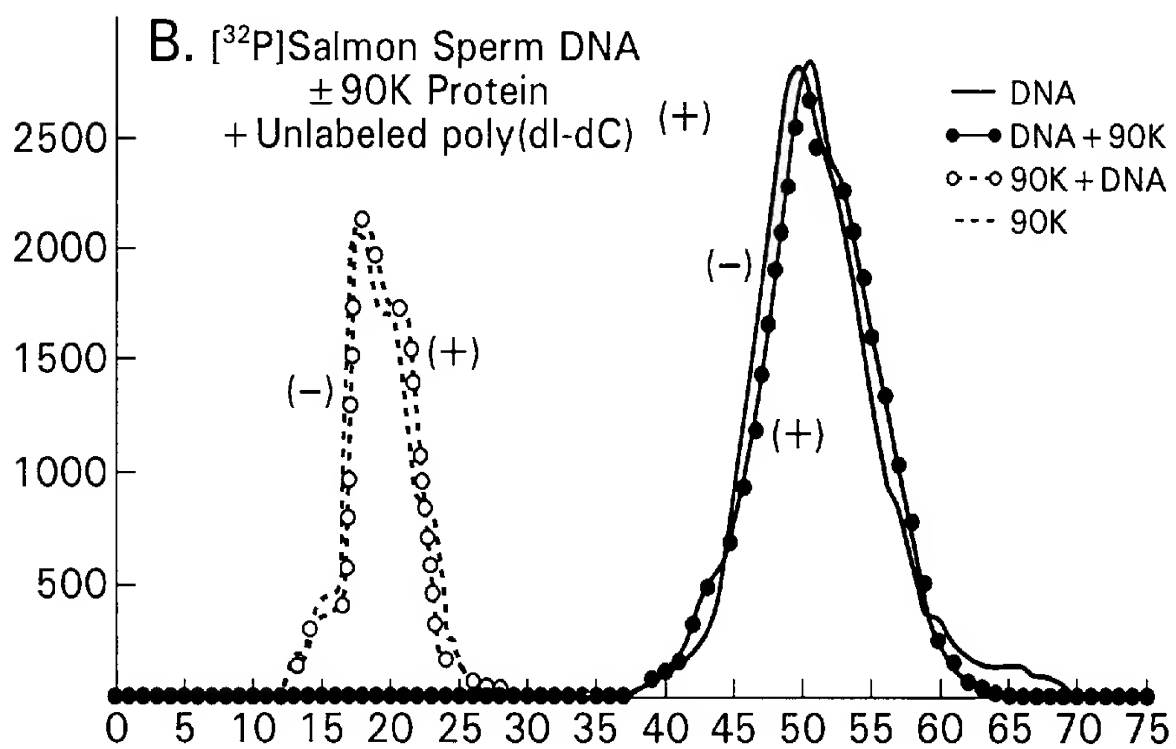
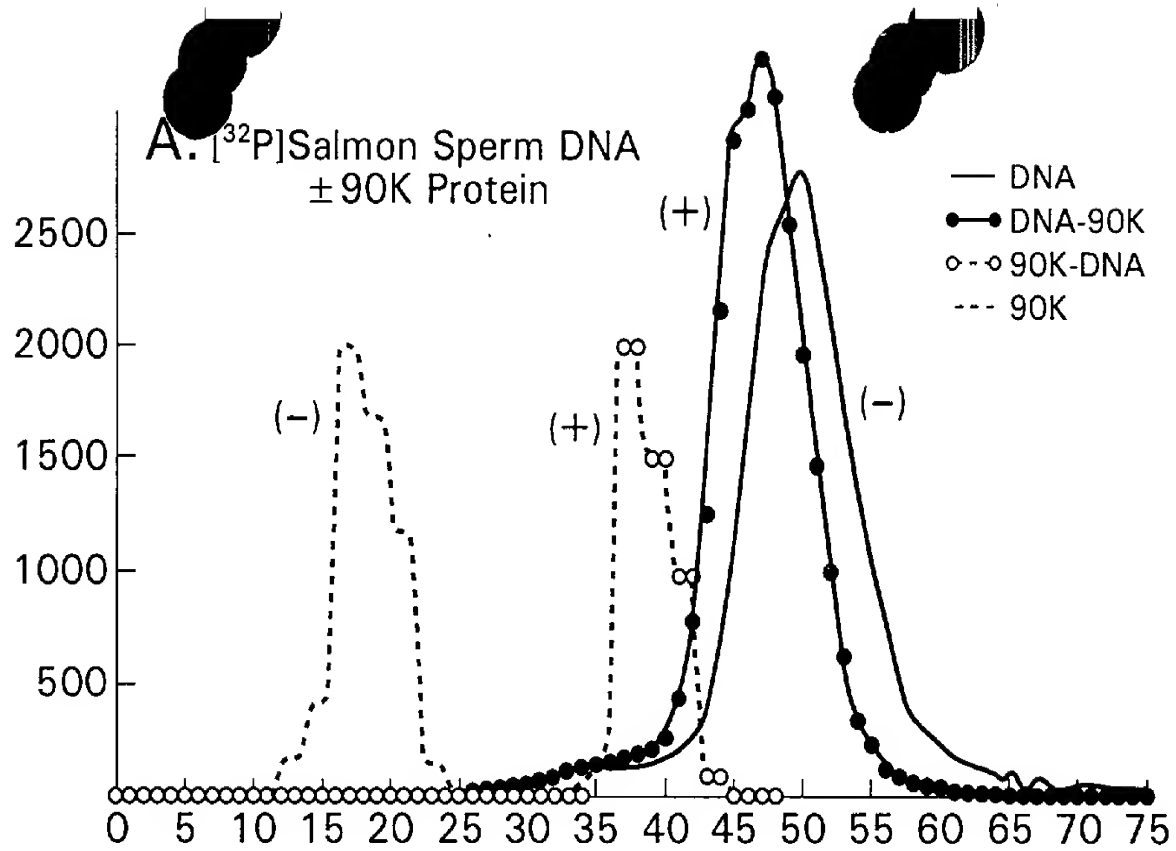


D



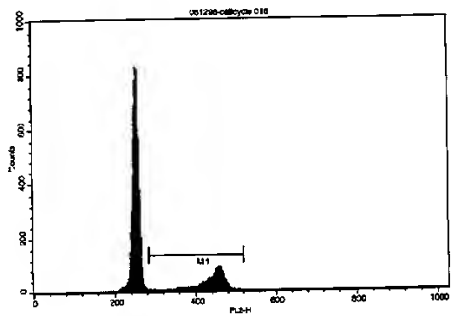


PROTEIN MEASURED BY ECL BLOT WITH ANTIBODY
(CPM)

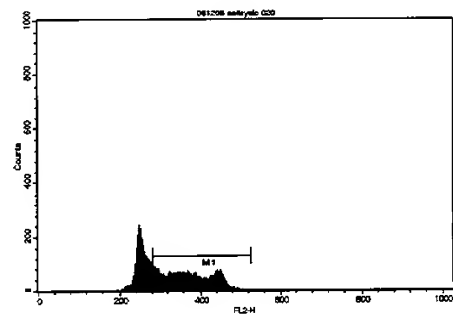


(%S+G2/M phase)

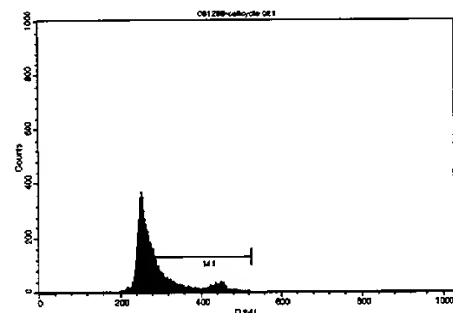
Control
(22.4%)



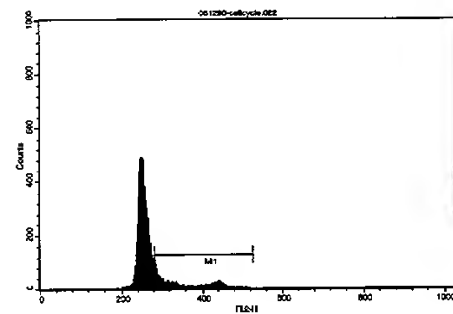
MMI
(58.3%)



MMI
+dsDNA
(35.6%)

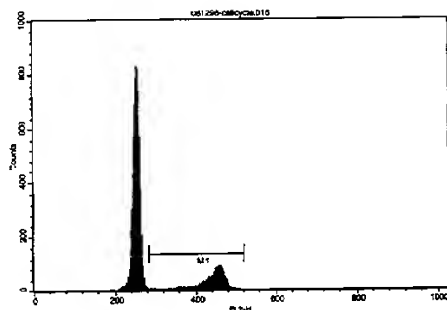


MMI
+dsRNA
(2.04%)

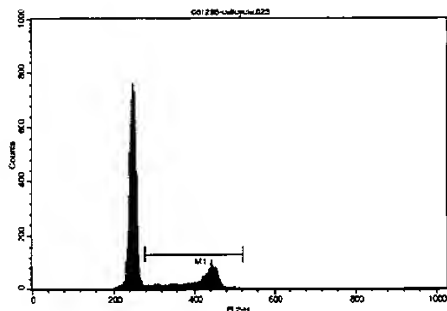


(%S+G2/M phase)

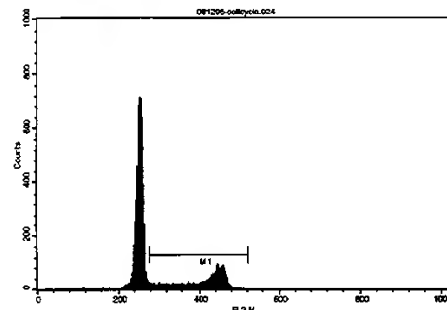
Control
(22.4%)



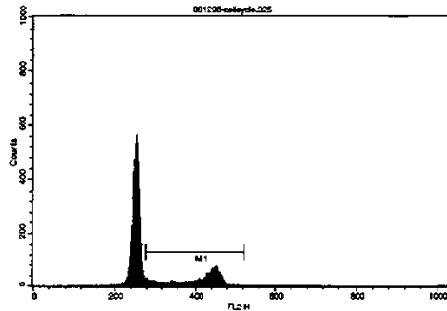
Comp#10
(26.8%)



Comp#10
+dsDNA
(29.2%)



Comp#10
+dsRNA
(29.9%)



Target Tissue
Triggering Event

Virus
Bacteria
Environmentally
Induced Damage
Oncogene Induced
Transformation

ds DNA
or
ds RNA
in Cytoplasm

Increased 90K
Imunostimulator

MMI or
Compound 10
Site of Action

Additional
Lymphocyte
Activation

Increased MHC Expression
in Target Tissue
(Class II > Class I)

Increased MHC Expression
in Target Tissue
(Class I > Class II)

Increased Expression
of Antigen
Presenting Genes in
Target Tissue

Lymphocyte
Recruitment
to Target Tissue
Lymphocyte
Activation

Bystander
Activation

MMI or
Compound 10
Site of Action

IFN- γ

IL-12
IGIF (IL-18)

Autoimmune
Disease